

Depending on the definition used, approximately 50% of patients satisfied criteria for engraftment syndrome. Earlier and more aggressive use of corticosteroids may be associated with less complicated post-transplant courses. Median overall survival has not been reached; the treatment related mortality was 3%. In addition, important clinical improvements and reductions in plasma VEGF levels can occur in the absence of significant decrease in the monoclonal protein. **Conclusions:** Unraveling the mechanisms of the syndrome both in the context of ASCT and in general are challenges for the future.

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### OUTCOME AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA IN PATIENTS WITH PRECEDING PLASMA CELL DISORDERS

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**Background:** Nearly a third of patients with newly diagnosed myeloma (MM) have a preceding diagnosis of plasma cell proliferative disorder (PCPD), mostly monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM) or plasmacytoma. While high dose therapy improves survival in patients with myeloma, it is not clear if patients with preceding PCPD have a different outcome. **Methods and Results:** We identified 151 patients with preceding PCPD from among 804 patients undergoing high dose therapy at our institution. These included 59 patients (7.3%) who had a preexisting diagnosis of MGUS, 88 (11%) patients, in whom the diagnosis of MM was preceded by SMM, including 23 patients who also had a preceding MGUS or plasmacytoma. In addition, 27 (3.4%) patients gave a preceding history of plasmacytoma. The median duration from the first diagnosis of a PCPD to that of myeloma was 32.4 months (range, 6.1 to 31 years), and was longer for patients with an initial diagnosis of MGUS compared to those with out preceding MGUS. While response rates including complete responses were generally similar between the two groups of patients, those with any preceding PCPD had a median TTP of 24.2 months (95% CI; 20, 28.3) compared to 17.3 (95% CI; 15.7, 18.8) months for those with no previous history (De novo Myeloma);  $p = 0.01$ . The median OS from transplant for patients with previous history was 63.7 months (95% CI; 50.2, 77.4) compared to 48.3 months (95% CI; 39.7, 56.9) for the de novo group,  $p = 0.01$ . These differences were most striking for those with a preceding diagnosis of MGUS; who had a longer time to progression (27.6 months vs. 17.7 months;  $p = 0.02$ ), and longer OS from transplant (80.2 months vs. 49.3 months,  $p = 0.046$ ) compared to those without any preceding MGUS. In a multivariate analysis, transplant within 12 months of diagnosis, lower serum M-protein at transplant, PCL  $<1\%$ , absence of cytogenetic abnormalities, achievement of CR, and presence of any preexisting monoclonal disorder prior to diagnosis of myeloma were independently prognostic for risk of post transplant relapse. **Conclusion:** Patients with preexisting PCPD at the time of myeloma diagnosis undergoing HDT has a better outcome reflecting more indolent disease and a favorable biology than those presenting with de novo myeloma and no antecedent plasma cell dyscrasia.

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### EARLY LYMPHOCYTE RECOVERY PREDICTS SUPERIOR SURVIVAL AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION IN NON-HODGKIN LYMPHOMA: A PROSPECTIVE STUDY

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**Background:** Day 15 absolute lymphocyte count (ALC-15)  $\geq 500$  cells/ $\mu$ l after autologous peripheral blood hematopoietic stem cell transplantation (APHSCT) is a significant predictor for survival. Limitations of previous reports have been their retrospective nature and no ALC-15 lymphocyte subsets analysis. Thus, from

2/2002 until 2/2007, 50 non-Hodgkin lymphoma (NHL) patients were enrolled in a prospective study to address these limitations. **Methods:** APHSCT eligible NHL patients who signed written consent for additional blood collections participated in the study. The primary end point was to confirm the ALC-15 survival role and to identify the lymphocyte subsets of greatest impact on ALC-15 after APHSCT. **Results:** The median age of the cohort was 57.7 years (range: 23–73). The groups (ALC-15  $\geq 500$  vs  $< 500$  cells/ $\mu$ l) were balanced to lymphoma type ( $p = 0.4$ ), gender ( $p = 0.5$ ), age ( $p = 0.2$ ), extranodal sites ( $p = 0.4$ ), lactate dehydrogenase ( $p = 0.5$ ), performance status ( $p = 0.5$ ), stage ( $p = 0.5$ ), international prognostic index ( $p = 0.9$ ), number of prior chemotherapies ( $p = 0.1$ ), clinical status at APHSCT ( $p = 0.2$ ), and infused CD34/kg ( $p = 0.8$ ). With a median follow-up of 22.2 months (range: 6–63.7 months), patients with an ALC-15  $\geq 500$  cells/ $\mu$ l ( $n = 35$ ) experienced superior overall survival (OS) and progression-free survival (PFS) compared with those who did not (median OS: not reached vs 19 months, 3 years OS rates of 80% vs 40%,  $p < 0.0004$ ; median PFS: not reached vs 3.4 months, 3 years PFS rates of 60% vs 14%,  $p < 0.0001$ , respectively). By day 15 post-APHSCT 30% of patients achieved a normal CD3, 18% a normal CD4, 38% a normal CD8, 4% a normal CD19, and 76% a normal [CD16+/56+/CD3-] counts. In Univariate analysis CD16+/56+/CD3- natural killer (NK) cells were the only ALC-15 lymphocyte subset that predicted for survival. Patients with a normal absolute NK cell count ( $\geq 80$  cells/ $\mu$ l,  $n = 38$ ) experienced superior OS and PFS compared with those who did not (median OS: not reached vs 5 months, 3 years OS rates of 76% vs 36%,  $p < 0.0001$ ; and median PFS: not reached vs 3 months, 3 years PFS rates of 57% vs 9%,  $p < 0.0001$ , respectively). **Conclusion:** This study confirms the prognostic ALC-15 survival role and identifies NK cells as the key lymphocyte subset affecting clinical outcomes after APHSCT in NHL. This study was supported in part by the Grant CA90628–04A from the National Institute of Health, and the University of Iowa/Mayo Clinic Lymphoma Spore CA97274.

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### AUTOLOGOUS STEM CELL TRANSPLANT (ASCT) IN FIRST REMISSION FOR PATIENTS WITH MANTLE CELL LYMPHOMA IS ASSOCIATED WITH PROLONGED SURVIVAL

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Mantle cell lymphoma (MCL) is associated with a median survival of less than 5 years and is incurable with conventional chemotherapy, therefore more aggressive therapy in the form of stem cell transplantation is often recommended. Patients receiving an autologous stem cell transplantation (ASCT) for MCL between 1993 and 2006 at Mayo Clinic Rochester were reviewed. 63 patients were identified, and their baseline characteristics at diagnosis included the following: median age 54 years (range 36–69), 51 are male, 12 are female; 55 patients had stage III or IV disease. The majority of patients had a good PS and low IPI. Median follow up from diagnosis is 59.8 months (range 15 months – 20.5 years) and from ASCT is 36.5 months (range 4 months – 10.8 years). Thirty-two patients underwent ASCT in first CR/PR and 31 patients in second or greater remission. Median overall survival (OS) from ASCT for the patients in first remission was 91.7 months and for the patients beyond first remission was 35.6 months ( $p = 0.01$ ). Median OS from diagnosis for the patients who underwent ASCT in first remission was 103.8 months and for the patients transplanted beyond first remission was 64.0 months ( $p = 0.17$ ). Median progression free survival (PFS) from ASCT was 29.6 months for the patients transplanted in first remission vs. 15.3 months ( $p = 0.03$ ) for the patients transplanted beyond first remission. Disease status at transplant appears to be the most significant factor affecting survival. Our data suggests that for patients in whom ASCT is being considered, it is advisable to proceed early in the disease (first remission) and not wait for relapse. Demonstration of improved cohort survival in those transplanted in first remission vs. a strategy of transplant at chemotherapy sensitive relapse would require a randomized prospective trial.